The Longwood Herbal Task Force
(http://www.mcp.edu/herbal/default.htm) and
The Center for Holistic Pediatric Education and Research
(http://www.childrenshospital.org/holistic/)

Chasteberry (*Vitex agnus castus*)

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Principal proposed uses: Corpus luteum insufficiency, premenstrual syndrome, mastalgia, and other menstrual problems

Other proposed uses: Lactagogue, menopausal symptoms, acne

Overview

Vitex agnus castus (Chasteberry) is a popular treatment for the management of female reproductive disorders including corpus luteum insufficiency, premenstrual syndrome (PMS), menopausal symptoms, and insufficient milk production. The German Commission E recommends it for menstrual problems, mastalgia, and premenstrual syndrome[1]. The specific chemical components responsible for its clinical effects have not been determined. One proposed mechanism is an effect on the pituitary's release of prolactin. Small randomized controlled trials indicate that vitex may be helpful in hyperprolactinemia, PMS and cyclical breast pain. Further research is needed to access its efficacy and safety for use by lactating mothers. There are no studies of its effects on menopausal symptoms or its safety in pregnancy. Side effects are rare and include rash, GI disorders, headache and increased menstrual flow.

Historical and Popular Uses

Chasteberry derives its common name from the belief that the plant inspires chastity. It was used in ancient Greece and Rome to diminish sexual desire. Monks in the Middle Ages used it for the same purpose, leading to its common name, "Monk's pepper". This purple-flowered shrub of the verbena family grows in the Mediterranean countries and central Asia.

A standardized preparation of chasteberry has been available in Germany since the 1950's, and is used to treat ovarian insufficiency and uterine bleeding[2]. The German

Commission E recommends vitex for the treatment for menstrual problems, mastalgia, and PMS[1]. It has been used to treat fibroid cysts and infertility[3], to stop miscarriages caused by progesterone insufficiency and to flush out the placenta after birth[4, 5]. German health authorities recommend its use for corpus luteum insufficiency, menopausal symptoms and inadequate milk production in nursing mothers[4]. It is used to treat acne in teenagers[6]. It has also been traditionally used as a digestive aid, sedative and anti-infective[3].

Botany

Medicinal species: Vitex agnus castus

Common names: Abraham's balm, chasteberry, chaste tree fruit, monk's pepper, safe tree, hemp tree, vitex

Botanical family: Verbenaceae

Plant description: A shrub or small deciduous tree that bears slender spikes of violet-blue, 8-10 cm flowers. The medicinal part of the plant is its peppercorn-sized fruit. The berries are aromatic and have a peppery taste[7].

Where it's grown: Asia, Europe (especially Mediterranean regions), North America

Biochemistry

Vitex Agnus Castus: Potentially Active Chemical Constituents

- Iridoid glycosides: agnoside, aucubin
- Flavonoids: casticin, kampferol, quercetagetin, vitexin[8]
- Progestins: progesterone, hydroxyprogesterone (flowers and leaves), testosterone, epitestosterone (flowers), androstenedione (leaves)[8]
- Alkaloids: viticin
- Volatile oil: 1,8-cineol, limes, linalool, terpinyl acetate,alpha pinenes and beta pinenes[9, 10]
- Essential fatty acids: palmitic acid, oleic acid, linoleic acid, stearic acid[10]

Vitex' precise mechanism of action and its active constituents have not been established[2]. Some constituents may have anti-inflammatory, sedative, and analgesic properties. Vitex also has dopaminergic properties, although it remains unclear which active compound is responsible.

The iridoid glycoside *aucubin* constituted 0.3% of vitex's leaves in one survey, and its *p*-hydroxybehzoyl derivative, *agnuside*, constituted 0.7%; unidentified glycosides constituted 0.07%[2].

The *flavonoid* content has been determined in chaste tree leaves (1.0-2.7%), flowers (1.0-1.5%) and fruits (0.5-1.0%)[8]. The berries contain 5% volatile oil.

Experimental Studies

***Vitex Agnus Castus:* Potential Clinical Benefits**
1. Cardiovascular: none
2. Pulmonary: none
3. Renal and electrolyte balance: none
4. Gastrointestinal/hepatic: none
5. Neuro-psychiatric: none
6. Endocrine: See Reproductive: hyperprolactinemia
7. Hematologic: none
8. Rheumatologic: none
9. Reproductive: Infertility, premenstrual syndrome, cyclic mastalgia, lactagogue, hyperprolactinemia, abnormal menstrual cycles
10. Immune modulation: none
11. Antimicrobial: Antibacterial and antifungal
12. Antineoplastic: none
13. Antioxidant: none
14. Skin and mucus membranes: Acne
15. Other/miscellaneous: none

1. **Cardiovascular:** none
2. **Pulmonary:** none
3. **Renal and electrolyte imbalance:** none
4. **Gastrointestinal/hepatic:** none
5. **Neuro-psychiatric:** none
6. **Endocrine:** See **Reproductive:** Hyperprolactinemia
7. **Hematologic:** none
8. **Rheumatologic:** none
9. **Reproductive**: Infertility, premenstrual syndrome, cyclic mastalgia, lactagogue, hyperprolactinemia, abnormal menstrual cycles. Numerous studies have investigated the use of vitex to treat symptoms of corpus luteum insufficiency such as irregular menstrual cycles,

dysfunctional uterine bleeding, mastodynia, and PMS[2]. There have been approximately four open human trials on vitex's use in hormone imbalance syndromes; all demonstrated positive results[3]. Clinical studies have focused on the treatment of PMS and mastodynia, and a few studies exist in patients with secondary amenorrhea, hyperprolactinemia, and corpus luteum insufficiency. Again, the results have been promising. There have been no clinical studies on the treatment of menopausal symptoms.

a. Infertility
   i. *In vitro data:* Vitex inhibited the spontaneous activity of the isolated rat uterus and did not demonstrate anti-fertility effects[11].
   ii. *Animal data:* none
   iii. *Human data:* In a randomized, prospective, placebo controlled double blind study, 96 women with fertility disorders took the vitex preparation Mastodynon® (30 drops twice a day) or placebo for three months. The outcome measures, which were a) pregnancy, b) spontaneous menstruation in women with amenorrhoea and/or subsequent pregnancy, or c) improved concentrations of luteal hormones, were achieved significantly more often in the Mastodynon group compared to the placebo group (57.6% versus 36.0%, p = 0.069). In women with amenorrhoea or luteal insufficiency, pregnancy occurred more than twice as often in the Mastodynon group as in the placebo group[12].

b. Premenstrual syndrome: Large open studies and several randomized controlled trials have shown conflicting results in the use of vitex to treat PMS symptoms.
   i. *In vitro data:* See endocrine.
   ii. *Animal data:* none
   iii. *Human data:* Case studies have noted an effect of vitex on premenstrual aggravations such as mouth ulcers, acne, and premenstrual edema[10]. A monograph on vitex noted a monitoring survey to study the effect of the liquid vitex extract Agnolyt® (40 drops daily) in 1542 women with PMS, ages 13 to 62. After an average of four months, both patients and physicians assessed the efficacy of treatment. Thirty-three percent of the patients reported total relief of their symptoms, and an additional 57% reported partial relief. Seventy-one percent of physicians reported good to very good efficacy

of treatment. Two percent of patients reported side effects including nausea, allergy, diarrhea, weight gain, giddiness, heartburn, hypermenorrhea, gastric complaints, acne, pruritus, erythema, alopecia, and cardiac palpitations. Seventeen of the 1542 women stopped the study due to side effects. Five hundred sixty-two patients continued to take Agnolyt after the monitoring period[13, 14].

In an open study (reported in a monograph on vitex), 36 patients with PMS who used 40 drops of Agnolyt daily for three months noted reductions in headaches, breast tenderness, bloating, fatigue, appetite, sweet cravings, nervousness, restlessness, anxiety, irritability, lack of concentration, depression, mood swings, and aggressiveness[13, 15].

A three-month randomized, placebo controlled study of 127 women, ages 18 to 45, with PMS compared Agnolyt® (one capsule daily containing 3.5-4.2 mg of a dried vitex extract) to vitamin B_6 (100 mg twice per day) for day 16-35 of the menstrual cycle. The vitex and vitamin B_6 groups had similar reductions in premenstrual tension syndrome scale scores (six typical premenstrual symptoms); 77% of those in the vitex group and 66% of those in the vitamin B_6 group had improvement in the clinical global impressions scale. Side effects included gastrointestinal and lower abdominal complaints (equally distributed between the two groups), skin reactions (two subjects in the vitex group) and transitory headache (one subject in the vitex group)[16, 17].

In a multicenter controlled double blind study, women ages 18 to 45 with PMS took a vitex tincture (1:5, 175 mg/day) or pyridoxine (200 mg/day). The total symptom score decreased comparably in the two groups[7, 18].

A randomized, double blind, placebo controlled study in 217 subjects with PMS compared vitex (600 mg capsules three times a day) to placebo for three months. Vitex was statistically more effective than placebo only in alleviating jitters and restlessness; there was no statistical significant difference for other PMS symptoms including impaired concentration, fluid retention, or pain[19].

No randomized controlled trials have compared long-term treatment with vitex to standard medical treatments such as birth control pills or antidepressants, or evaluated its interactions with standard treatment.

c. Cyclic mastalgia: Open studies and three placebo-controlled trials support the use of vitex in treating cyclic mastalgia.

i. *In vitro data:* See **Endocrine**.

ii. *Animal data:* none

iii. *Human data:* In an open study, 52 women with cyclic mastalgia took 30 drops of vitex extract twice a day for three months; most women reported disappearance or improvement of symptoms[3].

In a pilot study, 56 women with mastodynia who took a product containing chasteberry for three menstrual cycles had significantly reduced serum prolactin levels compared to those taking placebo[7].

In a randomized, double blind, crossover, placebo-controlled study in 20 women with cyclic mastalgia, women who received three months of treatment with Mastodynon® (a vitex extract) had significant relief of symptoms compared to those who took placebo[3, 20].

In a double blind, placebo controlled study of 100 women with cyclic breast pain, 1.8 ml of vitex extract daily for three months reduced menstrual associated breast pain[21].

d. Lactagogue

i. *In vitro data:* none

ii. *Animal data:* In healthy lactating rats, high doses of vitex reduced milk production significantly compared to controls[3]. On the other hand, other animal studies have found an increase in lactation and mammary enlargement[2].

iii. *Human data:* Two early studies found a favorable effect of vitex on milk production. A 1943 study found an increase in milk production in 80% of 125 patients[10]. In a 1957 controlled trial in 817 patients, there was a significant effect from vitex administration, with average milk production about three times that of controls after 20 days of treatment[10, 22].

e. Hyperprolactinemia (See also Abnormal menstrual cycles, below.)

i. *In vitro data:* Vitex inhibits prolactin release and binds to dopamine receptors[23-25]. It does not appear to inhibit the rat pituitary cell production of follicle stimulation hormone (FSH) or luteinizing hormone (LH)[23].

ii. *Animal data:* Vitex inhibited the secretion of prolactin in rats[24].

iii. *Human data:* In a placebo controlled crossover double-blind study of 20 healthy men, vitex had different effects on prolactin release at different concentrations. Men received doses of 120 mg, 240 mg or 480 mg of a special vitex extract (BP1095E1) daily for 14 days. There was a significant increase in prolactin level in men receiving the lowest dose, but a slight reduction in prolactin level in those receiving the higher doses[26]. There were no significant dose-dependent changes in the 24-hour serum prolactin profile. The changes that occurred during the treatment period depended on the baseline prolactin levels of the individual subjects[7].

See Abnormal menstrual cycles below for studies in women with hyperprolactinemia.

f. Abnormal menstrual cycles

i. *In vitro data:* none

ii. *Animal data:* none

iii. *Human data:* Numerous German open studies noted in the literature, including one dating back to the 1950's, have found a positive effect on vitex use in regulating the menstrual cycle[27-30].

In an open trial, 1,592 women (average age of 32) with corpus luteum insufficiency presenting as hypermenorrhea (418), polymenorrhea (359), secondary amenorrhea (202), dysmenorrhea (186), PMS anovulation (175), sterility (145), menorrhagia (66), and disturbed menstruation (32) received vitex extract (40 drops daily) for six months. Sixty one percent of the patients reported a good outcome, and physicians noted that 33% of patients were free of complaints and that there was a positive response to treatment in 51% of the patients[3, 31].

In a randomized double blind study, 52 women with menstrual cycle disturbances due to luteal phase defect and latent hyperprolactinemia received 20 mg

daily of Strotan® (an aqueous alcoholic extract of the vitex fruit) or placebo for three months. The subjects in the vitex group had a significant reduction in prolactin release, normalization of a shortened luteal phase, normalization of luteal progesterone synthesis, and significant reduction of their PMS symptoms compared to those receiving placebo. No side effects were reported[32].

10. **Immune modulation:** none
11. **Antimicrobial:** Antibacterial and antifungal
    i. *In vitro data:* Vitex demonstrated antimicrobial activity against *Staphylococcus aureus*, *Streptococcus faecalis*, *Salmonella species, Escherichia coli* (10-20%), *Candida albicans, C. tropicalis, C. pseudotropicalis*, and *C. krusei* (10-40%). Vitex extracts inhibited the growth of the dermatophytes and molds species: *Trichophyton mentagrophytes, Epidermophyton floccosum, Microsporum canis* and *M. gypseum*[33].
    ii. *Animal data:* none
    iii. *Human data:* none
12. **Antineoplastic:** none
13. **Antioxidant:** none
14. **Skin and mucus membranes:** Acne. A few clinical studies have investigated vitex' use in the treatment of acne[6, 34].
    i. *In vitro data:* none
    ii. *Animal data:* none
    iii. *Human data:* In a controlled trial of 161 acne patients, reported in a monograph on vitex, three months minimum treatment with vitex resulted in an improvement in 70% of patients, a result which was significantly better than placebo[10, 35].
15. **Other/miscellaneous:** none

Toxicity and Contraindications

All herbal products carry the potential for contamination with other herbal products, pesticides, herbicides, heavy metals, and pharmaceuticals, etc.

Furthermore, allergic reactions can occur to any natural product in sensitive persons.

Allergic reactions to vitex have not been reported.

Potentially toxic compounds in vitex: None known[7, 9].

Acute toxicity: Side effects are rare and may include itching, rash, headache, hair loss, fatigue, agitation, dry mouth, tachycardia, nausea and increased menstrual flow[2, 8]. There is one case report of mild ovarian hyperstimulation in a woman who self-prescribed vitex[36].

Chronic toxicity: Unknown

Limitations during other illnesses or in patients with specific organ dysfunction: Unknown

Interactions with other herbs or pharmaceuticals: There are no reports of herb-drug interactions involving vitex. Some herbalists believe that vitex could interfere with birth control pills, hormone replacement therapy, and other hormone replacement medication[2, 5]. Additionally, it has been hypothesized that individuals taking drugs classified as dopamine-receptor antagonists should use caution when taking vitex because animal studies indicate that vitex may interfere with the dopamine receptor[1, 4].

Safety during pregnancy, lactation and/or childhood: There are no clinical studies assessing the safety of vitex in children and pregnant women. Vitex is generally not recommended in pregnancy due to its unknown effects on the pituitary. There is insufficient information on the safety of using vitex during nursing. However, analysis for breast milk revealed no changes in composition[2].

Typical Dosages

Provision of dosage information dose NOT constitute a recommendation or endorsement, but rather indicates the range of doses commonly used in herbal practice.

Doses are given for single herb use and must be adjusted when using herbs in combinations.

Doses may also vary according to the type and severity of the condition treated and individual patient conditions.

A wide range of dosages are recommended by herbalists and used in clinical trails. Clinical trials to treat PMS have used anywhere from 3.5–4.5 mg/day of dried extract to 600 mg three times per day of dried fruit.

Examples of adult dosages:

Aqueous alcoholic extracts in 50-70% alcohol (v/v): Amount corresponding to 30-40 mg of dried fruit daily:

Fluid extract (1:1 g/ml): 0.03-0.04 ml daily

Tincture (1:5 g/ml): 0.15-0.2 ml daily

Dried extract (9.5-11.5:1 w/w): 2.6-4.2 mg daily[37]

Powdered extract: 175-225 mg chasteberry extract in tablet or capsule daily[16].

Whole fruit: 0.5-1.0 g three times daily[2]

Pediatric dosages: Unknown

Availability of standardized preparations: Standardized preparations used in Europe include Agnolyt®; Strotan®; and Mastodynon®. Examples of standardized products available in the US include Chaste Tree Berry Extract from Enzymatic Therapy, standardized to 0.5% agnuside; Power Herbs Chasteberry Power from Nature's Herbs, standardized to a minimum of 0.9% glycosides and combined with dong quai and Siberian ginseng; and a Nutritional Dynamics product standardized to 0.5% agnuside and 0.6% aucubin[16].

Dosages used in herbal combinations: Variable

See Also:

Vitex Clinician Information Summary: http://www.mcp.edu/herbal/vitex/vitex.cis.pdf

Vitex Patient Fact Sheet: http://www.mcp.edu/herbal/vitex/vitex.ph.pdf

REFERENCES

1. Blumenthal M. The complete German Commission E monographs : therapeutic guide to herbal medicines. Austin: American Botanical Council, 1998.
2. Newall CA, Anderson LA, Phillipson JD. Herbal medicines : a guide for health-care professionals. London: Pharmaceutical Press, 1996:ix, 296.
3. Christie S, Walker A. Vitex agnus castus, A review of its traditional and modern therapeutic use, current use from a survey of practitioners. The European Journal of Herbal Medicine 1997; 3:29 -45.
4. Peirce A. The American Pharmaceutical Association practical guide to natural medicines. New York: William Morrow and Company, Inc., 1999.
5. McGuffin M, Hobbs C, Upton R, Goldberg A. American Herbal Products Association's Botanical Safety Handbook. Boca Raton. New York: CRC Press, 1997:231.
6. Amann W. [Improvement of acne vulgaris following therapy with agnus castus (Agnolyt)]. Ther Ggw 1967; 106:124-6.
7. Schulz V, Hansel R, Tyler VE. Rational Phytotherapy: A Physicians' Guide to Herbal Medicine. Berlin: Springer, 1997:306.
8. Anonymous. Chaste Tree. In: Dombek C, ed. Lawerence Review of Natural Products. St. Louis: Facts and Comparisons, 1998.
9. Fleming T. PDR for herbal medicines. Montvale, NJ: Medical Economics Company, Inc., 1998.
10. Du Mee C. Vitex agnus castus. Aust J Med Herbalism 1993; 5:63-65.
11. Lal R, Sankaranarayanan A, Mathur VS, Sharma PL. Antifertility and Oxytocic Activity of Vitex-Agnus-Castus Seeds in Female Albino Rats. Bulletin of Postgraduate Institute of Medical Education and Research Chandigarh 1985; 19:44-47.
12. Gerhard I, Patek A, Monga B, Blank A, Gorkow C. Mastodynon(R) bei we iblicher Sterilit#t. Forsch Komplementarmed 1998; 5:272-278.
13. Brown D. Vitex agnus castus clinical monograph. Quarterly Review of Natural Medicine 1994; 06-30-94:111-121.
14. Dittmar F, Bohnert K. Premenstrual Syndrome: Treatment with a phytopharmceutical. TW Gynakol 1992; 5:60-68.
15. Coeugniet E. Premenstrual syndrome and its treatment. Arztezeitchr Naturheilverf 1986; 27:619-622.
16. Klepser T, Nisly N. Chaste Tree Berry for Premenstrual Syndrome. Alternative Medicine Alert 1999; June:64-67.
17. Lauritzen C, Reuter H, Repges R. Treatment of premenstrual tension syndrome with Vitex agnus castus: controled double blind study versus pyridoxine. *Phytomedicine*. 1997; 4:183-189.
18. Reuter H, al e. Die Therapie des pramenstrullen syndromes mit Vitex agnus castus. Kontrollierte doppelblindstrdie gegen pyridoxin. Z Pyhtotherapy Abstractband 1995:7.

19. Turner S, Mills S. A double-blind clinical trial on a herbal remedy for premenstrual syndrome; a case study. complementary therapies in medicine 1993; 1:73-77.
20. Kubista E, al e. Conservative treatment of mastitis. Z Gynakologie 1983; 105:1153-1162.
21. Halaska M, Raus K, Beles P, Martan A, Paithner KG. [Treatment of cyclical mastodynia using an extract of Vitex agnus castus: results of a double-blind comparison with a placebo]. Ceska Gynekol 1998; 63:388-92.
22. Mohr H. Clinical investigations of means to increase lactation. Dtsch Med Wschr 1954; 79:1513.
23. Jarry H, Leonhardt S, Gorkow C, Wuttke W. In vitro prolactin but not LH and FSH release is inhibited by compounds in extracts of Agnus castus: direct evidence for a dopaminergic principle by the dopamine receptor assay. Exp Clin Endocrinol 1994; 102:448-54.
24. Winterhoff H. *Arnzneiepflanzen mit endokriner Wirksamkei*. A Phytother. 1993; 14:83-94.
25. Sliutz G, Speiser P, Schultz AM, Spona J, Zeillinger R. Agnus castus extracts inhibit prolactin secretion of rat pituitary cells. Horm Metab Res 1993; 25:253-5.
26. Merz PG, Gorkow C, Schrodter A, Rietbrock S, Sieder C, Loew D, et al. The effects of a special Agnus castus extract (BP1095E1) on prolactin secretion in healthy male subjects. Exp Clin Endocrinol Diabetes 1996; 104:447-53.
27. Probst V, Roth O. On a plant extract with a hormone like effect. Dtsch Med Wschr 1954; 79:1271- 4.
28. Bleier W. Phytotherapy in irregular menstrual cycles or bleeding periods andothe gynecological disorders of endocrine origin. Zentralblatt Gynakol 1959; 81:701-9.
29. Losh E. Diagnosis and treatment of dyshormaonal menstrual periods in the general practice. Gynakol Praxis 1990; 14:489-495.
30. Propping D. Treatment of corpus leueum insufficiency. Zeits Allfemeinmedizin 1987; 63.
31. Propping D, al e. Vitex agnus castus tratment of gynacological syndromes. Therapeutikon 1991; 5:581- 5.
32. Milewicz A, Gejdel E, Sworen H, Sienkiewicz K, Jedrzejak J, Teucher T, et al. [Vitex agnus castus extract in the treatment of luteal phase defects due to latent hyperprolactinemia. Results of a randomized placebo-controlled double-blind study]. Arzneimittelforschung 1993; 43:752-6.
33. Pepeljnjak S, Antolic A, Kustrak D. Antibacterial and antifungal activities of the Vitex agnus-castus L. extracts. Acta Pharmaceutica Zagreb 1996; 46:201-206.
34. Amann W. [Acne vulgaris and Agnus castus (Agnolyt)]. Z Allgemeinmed 1975; 51:1645-8.
35. Giss G, al e. Haut-und Gesch 1968; 43:645.
36. Cahill DJ, Fox R, Wardle PG, Harlow CR. Multiple follicular development associated with herbal medicine [see comments]. Hum Reprod 1994; 9:1469-70.
37. Blumenthal M. Herbal medicine : expanded Commission E monographs. Austin, TX: American Botanical Council, 2000.